A novel protein-engineered hepatocyte growth factor analog released via a shear-thinning injectable hydrogel enhances post-infarction ventricular function.

Journal: Biotechnol Bioeng

Publication Year: 2017

Authors: Amanda N Steele, Lei Cai, Vi N Truong, Bryan B Edwards, Andrew B Goldstone, Anahita Eskandari, Aaron C Mitchell, Laura M Marquardt, Abbygail A Foster, Jennifer R Cochran, Sarah C Heilshorn, Y Joseph Woo

PubMed link: 28574594

Funding Grants: Injectable Hydrogels for the Delivery, Maturation, and Engraftment of Clinically Relevant Numbers of Human Induced Pluripotent Stem Cell-Derived Neural Progenitors to the Central Nervous System

Public Summary:
In the last decade, numerous growth factors and biomaterials have been explored for the treatment of myocardial infarction (MI). While pre-clinical studies have demonstrated promising results, clinical trials have been disappointing and inconsistent, likely due to poor translatability. In the present study, we investigate a potential myocardial regenerative therapy consisting of a protein-engineered dimeric fragment of hepatocyte growth factor (HGFdf) encapsulated in a shear-thinning, self-healing, bioengineered hydrogel (SHIELD). We hypothesized that SHIELD would facilitate targeted, sustained intramyocardial delivery of HGFdf thereby attenuating myocardial injury and post-infarction remodeling. Adult male Wistar rats (n = 45) underwent sham surgery or induction of MI followed by injection of phosphate buffered saline (PBS), 10 µg HGFdf alone, SHIELD alone, or SHIELD encapsulating 10 µg HGFdf. Ventricular function, infarct size, and angiogenic response were assessed 4 weeks post-infarction. Treatment with SHIELD + HGFdf significantly reduced infarct size and increased both ejection fraction and borderzone arteriole density compared to the controls. Thus, sustained delivery of HGFdf via SHIELD limits post-infarction adverse ventricular remodeling by increasing angiogenesis and reducing fibrosis. Encapsulation of HGFdf in SHIELD improves clinical translatability by enabling minimally-invasive delivery and subsequent retention and sustained administration of this novel, potent angiogenic protein analog.

Scientific Abstract:
In the last decade, numerous growth factors and biomaterials have been explored for the treatment of myocardial infarction (MI). While pre-clinical studies have demonstrated promising results, clinical trials have been disappointing and inconsistent, likely due to poor translatability. In the present study, we investigate a potential myocardial regenerative therapy consisting of a protein-engineered dimeric fragment of hepatocyte growth factor (HGFdf) encapsulated in a shear-thinning, self-healing, bioengineered hydrogel (SHIELD). We hypothesized that SHIELD would facilitate targeted, sustained intramyocardial delivery of HGFdf thereby attenuating myocardial injury and post-infarction remodeling. Adult male Wistar rats (n = 45) underwent sham surgery or induction of MI followed by injection of phosphate buffered saline (PBS), 10 mug HGFdf alone, SHIELD alone, or SHIELD encapsulating 10 mug HGFdf. Ventricular function, infarct size, and angiogenic response were assessed 4 weeks post-infarction. Treatment with SHIELD + HGFdf significantly reduced infarct size and increased both ejection fraction and borderzone arteriole density compared to the controls. Thus, sustained delivery of HGFdf via SHIELD limits post-infarction adverse ventricular remodeling by increasing angiogenesis and reducing fibrosis. Encapsulation of HGFdf in SHIELD improves clinical translatability by enabling minimally-invasive delivery and subsequent retention and sustained administration of this novel, potent angiogenic protein analog. Biotechnol. Bioeng. 2017;114: 2379-2389. (c) 2017 Wiley Periodicals, Inc.